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Award Number: DAMD17-01-1-0589

TITLE: The Effect of COX-2 Inhibitors on the Aromatase Gene
(CYP19) Expression in Human Breast Cancer

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REPORT DATE: June 2002

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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20030401 109

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE June 2002	3. REPORT TYPE AND DATES COVERED Annual (1 Jun 01 - 31 May 02)	
4. TITLE AND SUBTITLE The Effect of COX-2 Inhibitors on the Aromatase Gene (CYP19) Expression in Human Breast Cancer			5. FUNDING NUMBERS DAMD17-01-1-0589	
6. AUTHOR(S) : Charles L. Shapiro, M.D. William Burak, M.D. Robert Brueggemeier, Ph.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) The Ohio State University Research Foundation Columbus, Ohio 43210-1239 Email: shapiro-1@medctr.osu.edu			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) Aromatase (CYP-19) is responsible for estrogen biosynthesis within breast tumor tissue. Aromatase and cyclooxygenase-2 (COX-2) are both overexpressed in human breast cancer, and increased levels of prostaglandin (PG) activates the CYP19 promotor and increases gene expression. We hypothesize that celecoxib, a selective COX-2 inhibitor, will decrease PG, decrease the expression of CYP19, and reduce estrogen biosynthesis within tumor tissue. To test this hypothesis, in DOD grant # DAMD17-01-1-0589, tumor tissue will be collected from breast cancer patients at the initial diagnosis, and again at the definitive surgery (lumpectomy or mastectomy) for breast cancer. In the 10-14 day interval before the definitive surgery, patients will receive celecoxib and tissue samples collected before and after treatment with celecoxib will be evaluated for gene expression of COX-2 and CYP19. If our hypothesis is correct, then expression of the CYP19 gene will decrease in response to celecoxib. This study will provide preliminary data to a) support a mechanism whereby COX-2 inhibitors decrease estrogen production within breast tumors by decreasing CYP19 expression; and b) provide the rationale for initiating larger chemoprevention and therapeutic trials of COX-2 inhibitors in high risk and breast cancer patients.				
14. SUBJECT TERMS breast cancer			15. NUMBER OF PAGES 4	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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INTRODUCTION

This study will test the hypothesis that celecoxib, a selective Cox-2 inhibitor, will decrease PG, decrease the expression of CYP19, and reduce estrogen biosynthesis within tumor tissue. The primary objective of the study is to evaluate Aromatase (CYP19) and estrogen receptor (ER) gene expression by reverse-transcriptase polymerase chain reaction (RT-PCR) in response to a selective cyclooxygenase-2 (COX-2) inhibitor, celecoxib, in paired tumor tissue collected at the time of the initial diagnosis and at the time of definitive surgery for localized, non-metastatic breast cancer patients. The secondary objective is to evaluate the effect of celecoxib on the following biomarkers: estrogen receptor, progesterone receptor, Her-2/neu, Ki-67, COX-1, COX-2, CYP19, CD31, and PGE2, and Aromatase activity in paired tissue specimens by standard immunohistochemical methods. The study is approved by The Ohio State University IRB; however, is pending Army approval. In total, 34 subjects will be enrolled on the study. We anticipate that approximately 15 of the 34 subjects will be enrolled during the first year of the study.

BODY

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

KEY RESEARCH ACCOMPLISHMENTS

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

REPORTABLE OUTCOMES

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

CONCLUSIONS

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

REFERENCES

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

APPENDICES

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